REMARKS

The claims are 23-31.

Claim 11 (now claim 23) is objected-to as informal because of a parenthetical definition. The definition is deemed proper in that it specifies the meaning of the HL balance.

Claims 11-22 are rejected as obvious under 35 USC 103 over Akiyama (US'025) in view of Hauer (US'625), further in view of Reggio (US'169). The rejection is traversed. The claims have been re-drafted as 23-31. In the re-drafted claims the therapeutic agent has been limited to two cyclosporins, and component (a) has been limited to polyglycerol fatty acid esters.

US '025 is directed to a solid (at room temperature) matrix, the function of which is to adhere to the gastrointestinal mucosa so as to prolong the residence there of the active ingredient. An essential element of the matrix is a "viscogenic agent", e.g., acrylic acid polymers. US'025 does not concern itself with the problem of therapeutic agents which are sparingly soluble in water (e.g., the cyclosporins of the present invention). This can be seen from the broad range of agents listed at col. 6, lines 7-28 (none of which is structurally related to the cyclosporins). That the reference is not concerned with the problem of solubility is further demonstrated at col. 5, lines 53-54: "There is no particular limitation on the type of active ingredient." That the reference uses some components that are common in the pharmaceutical arts for a purpose different from that of the present invention is not the basis for an obviousness rejection.

US '625 is cited for its teaching that cyclosporins are known for their poor solubility and that various surfactants are known to be useful in cyclosporin formulations. However, this does not rectify the deficiency in the primary reference, as discussed above, since that reference does not address the issue of drug solubility. Further, there would be no motivation to combine these references since US '025 is directed to a solid which adheres to the gastrointestinal mucosa by incorporating as an essential element a viscogenic agent such as an acrylic acid polymer whereas the objective of US'625 is to provide a composition in the form of a microemulsion preconcentrate (see col. 5, lines 54-57). A person of ordinary skill in the art would not consider combining a teaching whose purpose is to prepare mucosa-adhering solid matrix composition with a teaching of a microemulsion preconcentrate. Lastly, US'625 teaches away from the present composition. The clinical trial described in US'625, col 32, compares 1) "Composition I" which comprises a hydrophilic component, a medium chain fattay acid triglyceride, and a hydrophilic surfactant, and 2) "Composition X", which comprises a hydrophilic component, an oil, and a lipophilic surfactant. The clinical trial shows improved bioavailability and reduced variability of Composition I over Composition X, thus teaching away from the presently claimed compositions which comprise a lipophilic surfactant as an essential ingredient.

The rejection is made further in view of Reggio (US'169). The Examiner's reliance on Reggio is deemed improper. This reference concerns chewing gum, specifically a formulation with enhanced film-forming properties; i.e., a better bubble gum composition. Such a disclosure is totally irrelevant to one of ordinary skill in the art of preparing pharmaceutical formulations; i.e., the subject of the present invention.

Claims 11-22 are rejected under 35 USC 103 as obvious over Hahn in view of Hauer (US'625), further in view of Reggio (US'169). The rejection is traversed. Hahn is a PhD thesis whose purpose is: "...to investigate the solubilization of tensides ... and then ... to select and possibly optimize suitable compounds." (para. 2, bridging pp 2/3). There is nothing in Hahn which would lead one of ordinary skill in the art to the composition of the present invention, i.e., a composition which recites a carrier composition comprised of specific amounts of polyglycerol fatty acid esters, triglycerides, and non-ionic surfactants. The comments *supra* regarding Hauer and Reggio are incorporated herein. There is no motivation in any of the documents for their combination with any reasonable expectation of achieving the desired results, i.e. cyclosporin-containing compositions with enhanced solubility, resorptive capacity, and bioavailability. It is deemed that the combination of these references does not make obvious the present invention.

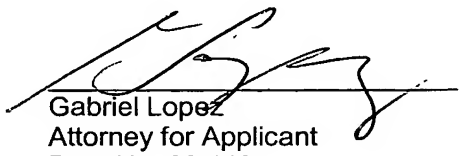
Claims 11-22 are rejected under 35 USC 103 as obvious over Hauer (US'625), with an additional comment regarding Reggio (US'169). The rejection is traversed. The comments *supra* regarding Hauer and Reggio are incorporated herein. It is deemed that the combination of these references does not make obvious the present invention.

Regarding the rejection of the process claims on the basis that merely mixing ingredients is *prima facie* obvious, this would only be true if the selection of the ingredients to be mixed is obvious and results of said mixing is obvious. In the present case, for the reasons provided above, there is nothing obvious about the selected compounds nor the desired results, i.e. cyclosporin-containing compositions with enhanced solubility, resorptive capacity, and bioavailability.

It is requested that the amendment be entered and that the Examiner reconsider the rejections in view of the amendment and remarks and that the case be passed to issue.

A three-month extension is hereby requested for filing a response. Please charge Deposit Account No. 19-0134 in the name of Novartis Corporation in the amount of $**930** for payment of the extension fee. The Commissioner is hereby authorized to charge any additional fees under 37 CFR §1.17 which may be required, or credit any overpayment, to Account No. 19-0134 in the name of Novartis.

Respectfully submitted,



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Date: 7/15/03